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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,621	12/11/2003	Atul Varadhachary	HO-P02705US2	8531
26271	7590	10/31/2006	EXAMINER	
FULBRIGHT & JAWORSKI, LLP			KAM, CHIH MIN	
1301 MCKINNEY			ART UNIT	
SUITE 5100			PAPER NUMBER	
HOUSTON, TX 77010-3095			1656	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/733,621

Applicant(s)

VARADHACHARY ET AL.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-22 and 35-53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-22 and 35-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. The Request for Continued Examination (RCE) filed on September 26, 2006 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

#### ***Status of the Claims***

2. Claims 1, 3-22 and 35-53 are pending.

Applicants' amendment filed on September 26, 2006 is acknowledged. Applicants' response has been fully considered. Claims 1, 6 and 8 have been amended, and new claims 39-53 have been added. Thus, claims 1, 3-22 and 35-53 are examined.

#### **Withdrawn Claim Objections**

2. The previous objection to claim 38 is withdrawn in view of applicant's response at page 7 of the amendment filed September 26, 2006.

#### **Withdrawn Claim Rejections - 35 USC § 112**

3. The previous rejection of claim 6 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claim, and applicant's response at page 6 of the amendment filed September 26, 2006.

#### **Withdrawn Claim Rejections - 35 USC § 103**

4. The previous rejection of claims 1, 3-7 and 11-22 under 35 U.S.C. 103(a) as being obvious over Kruzel *et al.* (US 2003/0096736), is withdrawn in view of applicant's amendment to the claim, and applicant's response at page 7 of the amendment filed September 26, 2006.

#### **Withdrawn Claim Rejections-Obviousness Type Double Patenting**

5. The previous rejection of claims 1, 3-22 and 35-37 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 12 of copending

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Application No. 10/862,213, is withdrawn in view of a terminal disclaimer filed, and applicant's response at page 7 of the amendment filed September 26, 2006.

6. The previous rejection of claims 1, 3-7, 11-13, 15-17, 20-22 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 13-17, 24, 28, 42-50 and 73-79 of copending Application No. 10/434,769, is withdrawn in view of a terminal disclaimer filed, and applicant's response at page 7 of the amendment filed September 26, 2006.

***New Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-22 and 35-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating pain in a subject suffering from pain, comprising administering to the subject an effective amount of a lactoferrin composition comprising lactoferrin or an N-terminal lactoferrin variant, wherein the pain is associated with cancer or surgery, and wherein the variant has a deletion or substitution of 1 to 16 N-terminal amino acid residues of lactoferrin and has the same biological function as the full length of lactoferrin as indicated in paragraphs [0034] and [0054]; or a method of treating a patient suffering from a recurrence of gastric cancer after a surgical operation using lactoferrin as indicated in the prior art, does not reasonably provide enablement for a method of treating pain in a subject suffering from pain, comprising administering to the subject an effective amount of a lactoferrin composition or a lactoferrin composition comprising an N-terminal lactoferrin

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variant, wherein the pain is associated with cancer or surgery, but the lactoferrin composition or the structure and function of the N-terminal lactoferrin variant in the composition is not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 3-22 and 35-53 are directed to a method of treating pain in a subject suffering from pain, comprising administering to the subject an effective amount of a lactoferrin composition or a lactoferrin composition comprising an N-terminal lactoferrin variant, wherein the pain is associated with cancer or surgery. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the instant invention is directed to a method for reducing acute or chronic pain, the method comprising administration of a lactoferrin composition, either alone or in combination with other therapies, where the lactoferrin composition comprises lactoferrin or an N-terminal lactoferrin variant in which at least the N-terminal glycine residue is truncated or substituted, or lactoferrin lacking one or more N-terminal residues or having one or more substitutions in the N-terminal (pages 2-4; paragraph [0034]). There are no indicia that the present application enables the full scope in view of the method of treating pain using a lactoferrin composition as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance to enable the full scope of the claims. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability

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or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the lactoferrin composition or the N-terminal lactoferrin variants in the composition, which is not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 1-4 illustrate the use and effect of lactoferrin in mice with heat-, phenylquinone- or formalin-induced mice; Examples 5-7 illustrate using lactoferrin in the reduction of pain in patients with cancer, surgery or severe osteoarthritis. However, there are no other working examples indicating the effects of various N-terminal lactoferrin variants in the treatment of pain in patients having cancer or surgery.

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., Nuijens et al., U.S. patent 6,333,311) teach lactoferrin variants with one or more arginine residues in the N-terminal region deleted are used for treating inflammation. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of functional N-terminal lactoferrin variants and their effects in the treatment of pain to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method for treating pain in subjects suffering pain, comprising administering to the subject an effective amount of a lactoferrin composition or a lactoferrin

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composition comprising an N-terminal lactoferrin variant, wherein the pain is associated with cancer or surgery. While the specification indicates the use of specific N-terminal lactoferrin variant having a deletion or substitution of 1 to 16 N-terminal amino acid residues of lactoferrin and having the same biological function as the full length of lactoferrin (See paragraphs [0034] and [0054]) in treating pain, the specification has not demonstrated the effects of various N-terminal lactoferrin variants, in which the structure and function are not defined, in the treatment of pain, the invention is highly unpredictable regarding the structures of functional N-terminal lactoferrin variants and their effects in the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating pain in subjects suffering pain, comprising administering to the subject an effective amount of a lactoferrin composition or a lactoferrin composition comprising an N-terminal lactoferrin variant, wherein the pain is associated with cancer or surgery. While the specification discloses the use and effect of lactoferrin in mice with heat-, phenylquinone- or formalin-induced mice (Examples 1-4), and the use of lactoferrin in the reduction of pain in patients with cancer, surgery or severe osteoarthritis (Examples 5-7), the specification does not demonstrate the effects of various lactoferrin variants or N-terminal lactoferrin variants in the treatment of pain. Besides the lactoferrin and specific N-terminal variants of lactoferrin (See paragraphs [0034] and [0054]), the specification does not indicate any lactoferrin variant can be used in the treatment, thus one of skilled in the art would not know how to make and use a lactoferrin composition comprising a lactoferrin variant.

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Therefore, it is necessary to carry out undue experimentation to identify a functional lactoferrin variant or an N-terminal variant of lactoferrin in treating pain.

(6). Nature of the Invention

The scope of the claims encompass pain in subjects suffering pain, comprising administering to the subject an effective amount of a lactoferrin composition, however, the specification does not provide sufficient teachings on the use of a lactoferrin variant in treating pain. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods associated with variants, the structure and effect of a lactoferrin variant is unpredictable, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify a functional lactoferrin variant and to assess its effect in the treatment.

8. Claims 38-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38-53 are directed to a method of treating a subject suffering from pain comprising the step of administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject within 60 minutes of administration, wherein the pain is associated with cancer or surgery. While the specification indicates that oral lactoferrin treatment resulted in a statistically significant reduction in pain as



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measured by number of tail flicks at 60 min observed in mice with heat-induced pain (see Example 1; paragraph [0098]; Fig. 1) and oral lactoferrin treatment resulted in reduction in pain as measured by number of writhes at 60 min observed in mice with phenylquinone-induced pain (see Example 2; paragraph [0099]; Fig. 2), the specification does not disclose administration of a lactoferrin composition provide improvement in pain in the subject within 60 min minutes of administration, when the pain is associated with cancer or surgery. The lack of description on the pain reduction in the subject by administering a lactoferrin composition, when the pain is associated with cancer or surgery, and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

***Maintained Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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9. Claims 1, 3-6, 11, 15, 16 and 18-22 remain rejected under 35 U.S.C. 102(e) as being anticipated by Ando *et al.* (US 2004/0018190, filed on November 22, 2001).

Ando *et al.* teach lactoferrin tablets were produced by mixing 50 mg of lactoferrin powder with lactose, cellulose and carboxymethylcellulose calcium salt in a dry state (Example 7), and enteric lactoferrin tablets were administered to a patient suffering from a recurrence of gastric cancer after a surgical operation and retention of cancerous abdominal fluid (paragraph [0056]). In this case, the abdominal fluid was drawn several times a week to relieve pain, after orally taking enteric lactoferrin tablets (lactoferrin dose: 0.45 g per day) for a week, the abdominal fluid was completely absorbed and eliminated (claims 1, 3, 4, 11, 15, 18 ad 19). The reference also indicates lactoferrin can be obtained from bovine milk (paragraphs [0011], [0017]; claim 5 and 6), and enteric lactoferrin tablets can deliver the lactoferrin to the lower digestive tract (the duodenum and small intestine; paragraph [0021]; claim 16). Although the reference does not specifically indicate administration of lactoferrin reduces the production or activity of pro-inflammatory cytokines or enhances the production or activity of some cytokines, since the reference teaches the same method steps, it would be expected that administration of lactoferrin would have produced these effects (claims 20-22).

#### Response to Arguments

Applicants indicate the claims have been amended to specify pain from surgery, and Ando does not disclose treatment of surgical patients. Applicant requests the rejection be withdrawn. (page 7 of the response).

Applicants' response has been considered, however, the arguments are not persuasive because Ando teaches use of lactoferrin to treat a patient with a recurrence of gastric cancer after

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a surgical operation and retention of cancerous abdominal fluid, and administration of lactoferrin can eliminate the abdominal fluid and relieve the pain, which meet the criteria of the claimed invention. Therefore, the rejection is maintained.

***Conclusion***

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.  
Primary Patent Examiner



CHIH-MIN KAM  
PRIMARY EXAMINER

CMK

October 27, 2006